

DRAFT: SCOTTISH GOOD PRACTICE STATEMENT ON ADULTS WITH ME-CFS:
QUICK REFERENCE GUIDE

Purpose

The purpose of this Scottish Good Practice Statement on ME-CFS is to provide general practitioners with a simple, straightforward document that can be easily used in the consulting room to assist with the diagnosis and clinical management in Primary Care of adults with ME-CFS of differing degrees of severity. The statement is primarily based on synthesis of best available current evidence¹. It is therefore a 'living' document and will be subject to periodic review as the evidence base evolves. It should be noted the statement offers guidance and should not be regarded as prescriptive; such general advice will always require to be modified in line with needs of any individual patient. This document is accompanied by a 'Patient Guide for Adults' and a detailed document entitled 'Scottish Good Practice Statement on ME-CFS'.

Prevalence

The condition has a prevalence of around 5 per 1000. A GP will have ~7 patients with the condition in an average list size. It is more common in women and in patients aged from 35-55.

Clinical evaluation of ME-CFS

Initial Presentation

This may be sudden or gradual, following viral infections, other physical illnesses, stressful events or without precipitant. The illness usually presents with a combination of persistent or recurrent fatigue and myalgic pain, in the absence of swelling or redness, that can be migratory. The symptoms are provoked by physical or mental exertion. Post-exertional malaise lasting more than 24 hours is commonplace. There is a substantial reduction in activity levels.

As with any long term condition, early and accurate diagnosis brings significant benefits. The aim should be to make a provisional diagnosis by 3-4 months into the illness.

It is helpful to create a list of all current symptoms as 'polysymptomatology' is a significant diagnostic clue. Subjective cognitive impairments, particularly slowed speed of processing, poor attention and disturbances of anterograde memory, are almost always present. Recurrent 'flu-like' symptoms, sore throats, painful swollen lymph nodes, sleep disturbance (hypersomnia, insomnia and unrefreshing sleep) and headaches (usually tension-type) are common associated symptoms. Other symptoms include peri-oral and peripheral paraesthesia, postural light headedness, dizziness, palpitations, nausea, irritable bowel symptoms, urinary frequency and urgency, feelings of fever and shivering, and altered appetite and weight.

Enquire about travel, tick bites, 'odd' infections, drug and alcohol use. Review current prescribed medications.

Some patients presenting with complaints of persistent fatigue and/or pain will have somatization disorder.

Mental state examination should be undertaken on all patients. Major depressive disorder and panic disorder with agoraphobia can be the sole cause of persistent fatigue or present as important, and reversible, comorbid disorders in ME-CFS. Questions should be tailored enquiring about the ability to enjoy anything (including those activities the patient is physically capable of) and 'situationally-specific' somatic symptoms of panic (ie chest pain, palpitations, dizziness, weakness after a typical time gap on leaving the house).

Examination: a full physical examination should be performed including:

- height & weight (severe obesity can cause fatigue)
- erect and supine blood pressure (to exclude significant postural hypotension which can mimic some of the symptoms of ME-CFS or be a sign of Addison's);
- general medical examination, including looking for signs of anaemia, tanning in unusual sites (for Addison's), enlarged or tender lymph nodes and organomegaly;
- skin and joints for evidence of systemic inflammatory diseases. Note any peri-articular tenderness typical of fibromyalgia.
- a neurological examination to exclude objective neurological abnormalities such as obvious wasting, ptosis, upper motor neuron signs, ataxia, fasciculations, absent reflexes. NB Muscle twitches and spasms are common occurrences in ME-CFS and some 'give-way' weakness is also common (because of pain or fatigue) but normal power is usually possible even if only for a few seconds with encouragement.

Features suggestive of other disorders or requiring further investigation

Fatigue is a symptom of many diseases and therefore a definitive list is not possible. The following should be regarded as 'red flags' for alternative diagnostic explanations, as part of the process of differential diagnosis

- Substantive unexplained weight loss
- Objective neurological signs
- Symptoms or signs of inflammatory arthritis or connective tissue disease
- Symptoms or signs of cardio-respiratory disease
- Symptoms of sleep apnoea
- Clinically significant lymphadenopathy

Investigations

All patients

Blood tests: FBC, U&Es and creatinine, LFTs (including albumin), TFTs, glucose (random), ESR, C reactive protein, calcium, creatine kinase. **Other:** urinalysis.

When indicated by history or examination

Blood tests: AMA (if minor alterations in LFTs), ANA, CMV, coeliac serology (if diarrhoea, weight loss or history of auto-immune disorders), EBV, ENA, HIV, Hepatitis B&C, Lyme, serology for chronic bacterial infections, Toxoplasma. **Other:** ECG (if any cardiological symptoms).

Investigations not currently indicated in clinical practice

Blood tests: B12 & folate (where normal FBC), candida albicans, ferritin, fibrinogen, lactate dehydrogenase, mitochondrial testing, platelet activation, protein electrophoresis, prothrombin fragment 1&2, soluble fibre monomer, thrombin-antithrombin complexes, XMRV serology. **Other:** Auditory brainstem responses, EEG, electrodermal activity, MRI brain scan (in the absence of objective neurological signs), SPET imaging, PET imaging, Tilt table testing (in the absence of other clinical indications).

Interventions, Management and Rehabilitation

All patients will benefit from the general skills of good medical practice including being treated with respect, being listened to with empathy, and having the opportunity to build a rapport with their general practitioner. All treatment should be collaborative and there is no place for a coercive approach.

Encourage early rehabilitation. In particular, encourage activity based on rehabilitation principles.

Treatment for associated clinical conditions, such as tension headache, irritable bowel syndrome or depression should follow standard clinical practice. Pain symptoms are often problematic. Avoid excessive use of opiate analgesics and consider 'atypical' analgesics like tricyclics, gabapentin and duloxetine. Be alert to the problems of polypharmacy and stop medications that are not producing substantive benefits.

Many patients and clinicians favour an approach based on self management, called 'pacing'. The clinical effectiveness of this strategy is presently being tested in a large RCT.

Evidence levels for Interventions: The grading of level of evidence has been made in accordance with the SIGN Guidelines approach. In keeping with recent SIGN developments, due weight is also given to people's experience of living with the condition. Further details are available at: <http://www.sign.ac.uk/guidelines/fulltext/50/annexb.html>

Interventions that benefit some, but not all:

Level 1 evidence:

- Cognitive Behavioural Therapy (when delivered in centres with specific expertise in treating ME-CFS)
- Graded Exercise Therapy (when delivered in centres with specific expertise in treating ME-CFS)

Level 4 evidence:

- Acupuncture
- Gabapentin
- Pacing
- 'Step 1' analgesics
- TENS
- Tricyclic antidepressant drugs (starting with low dose)

Interventions that possibly work and are unlikely to do harm (Level 2-)

- Acetyl-L-carnitine and propionyl-L-carnitine supplements
- Essential fatty acid supplements
- Massage therapy
- Melatonin

Interventions that may do more harm than good (Level 4)

Amantadine, antifungal drugs, baclofen, benzodiazepines, methylphenidate, naltrexone, nimodipine, thyroxine (except where low T4 levels), non specific advice on activity (eg "go to the gym and do some exercise").

Interventions that do more harm than good (Level 2-)

Immunoglobulins, oral NADH, Staphylococcus toxoid.

Interventions for which trials have shown a lack of benefit (level 2- and above)

Acyclovir, acyclidine, alpha interferon, amino acids, ampligen, clonidine dexamphetamine, fludrocortisones, fluoxetine, galantamine, ganciclovir, general supplements, growth hormone, homeopathy, hydrocortisone, inosine pranobex, interferon, liver extract, low sugar/low yeast diet, magnesium, medicinal mushrooms, moclobemide, osteopathy, phenelzine, pollen extracts, selegiline, sulbutiamine, terfenadine, topical nasal corticosteroids.

Prognosis

The prognosis is variable. The majority of patients will show some degree of improvement over time, especially with treatment, although many will pursue a fluctuating course with periods of relative remission and relapse. Patients in primary care also present with milder fatigue states that have a much more favourable prognosis. However there is a significant minority, who are severely affected for many years, and in extreme cases for decades.

Reference

1 Bagnall AB, Hempel S, Chambers D, Orton V, Forbes C. *The treatment and management of chronic fatigue syndrome/ myalgic encephalomyelitis in adults and children*. Centre for Reviews and Dissemination, University of York. February 2007.

Key Guiding Principles:

- **WORK IN PARTNERSHIP WITH THE PATIENT**
- **MUTUALLY AGREE ALL TREATMENTS**

Patient presents with symptoms that may indicate ME-CFS

Do an initial assessment

- Take history (including exacerbating and relieving factors, sleep disturbance, inter-current stressors)
- Conduct physical examination
- Look for signs of depression and/or agoraphobic symptoms

Reassessment and interim advice

- Remain vigilant for newly emerging symptoms suggestive of alternate diagnoses.
- Maintain relationship and encourage discussion of mood state. Be particularly vigilant for somatic symptoms of depression and agoraphobic symptoms.
- Encourage early rehabilitation. In particular encourage activity based on rehabilitation principles. Suggest use of a diary & planned activity, *within abilities*, setting achievable goals. Be alert for, and caution against, a 'boom and bust' approach such as doing all the week's housework on a 'good day' then collapsing the next day

Arrange Investigations

- FBC, U&Es, creatinine, LFTs (inc albumin), TFTs, ESR, CRP, calcium, creatine kinase, random glucose, urinalysis.
- Consider whether any other investigations are indicated by history

Make provisional diagnosis

- In adults if symptoms have lasted 4 months and other diagnoses have been excluded
- Reconsider diagnosis if any 'red flag' symptoms/signs are present

ME-CFS diagnosis not supported at this stage: Consider referral to appropriate medical or psychiatric clinic

- If specific diagnostic query (such as possible MS)
- If substantial pre-existent co-morbidity

If ME-CFS suspected -

- and symptoms have lasted more than four months and not improving
- or presentation is severe -

consider referral to Specialist Clinic/ Treatment Centre for:

- assessment
- further investigation as appropriate
- management advice
- referral for specific treatments if appropriate
- an expert intervention package tailored to the needs of each individual patient.

Maintain general practice involvement after specialist referral and follow general principles of good medical care

Review management plans and progress

- Remember to seek out positive features, such as goals met and achievements

Help manage setbacks and relapses